

("U.S. '050"), or International Patent Application No. WO 82/03772 ("WO 82/03772"), in view of European Patent No. 619370 ("EP 619370"), U.S. patent No. 5,589,451 ("U.S. '451"), U.S. Patent No. 5,814,605 (U.S. '605"), International Patent Application No. WO 97/13857 ("WO 97/13857"), or International Patent Application No. WO 98/16243 ("WO 98/16243"). The Examiner asserts that the references teach the use of plasminogen and KFG **separately** in pharmaceutical formulations and that it would have been *prima facie* obvious to combine the two ingredients.

Applicants respectfully assert that it would not have been obvious to combine plasminogen (which is a protease enzyme), with KFG (which is a growth factor protein). **Although pharmaceutical formulations have previously used protease enzymes and growth factor proteins independently, their simultaneous use is counter-intuitive. Protease enzymes degrade proteins.** *See*, Specification, Page 9, lines 7 – 18.

The current application utilizes a unique **combination of a protease enzyme and a growth factor protein** to produce a synergistic effect previously unknown, unanticipated, and contrary to the common wisdom of those of skill in the art. The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *See In re Mills*, 916 F.2d 680, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). None of the cited references suggests the desirability, or even the feasibility, of combining a protease enzyme and a growth factor protein.

For these reasons, Claims 1, 3, 5, 7, 13 – 15, 17, and 23 – 25 are patentable over EP 307847, U.S. '050, or WO 82/03772, in view of EP 619370, U.S. '451, U.S. '605, WO 97/13857, or WO 98/16243.

## **II. Conclusion**

Applicants respectfully submit that, in light of the foregoing comments, Claims 1, 3, 5, 7, 13 – 15, 17, and 23 – 25 are in condition for allowance. A Notice of Allowance is therefore requested.

Attorney Docket No.:  
CARR-0084 (103216.00252)

PATENT

If the Examiner has any other matters which pertain to this Application, the Examiner is encouraged to contact the undersigned to resolve these matters by Examiner's Amendment where possible.

Respectfully submitted,



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January 21, 2004  
Date